

LISTING OF CLAIMS

This listing of claims will replace any previous listing of claims in this case.

1-7. **(Canceled)**

8. **(Previously presented)** A method for preparing an agent that effects a biological event mediated by the association of two or more endogenous cell surface receptor molecules, the method comprising preparing an agent which includes a first non-peptidic moiety that binds to one of the cell surface receptor molecules covalently linked to a second non-peptidic moiety that binds to the other cell surface receptor molecule, wherein the agent binds to both cell surface receptor molecules.

9. **(Previously presented)** The method of claim 8 wherein the biological event is mediated by the association of two or more molecules of the same cell surface receptor and the first and second non-peptidic moieties are the same.

10. **(Previously presented)** The method of claim 9 wherein the cell surface receptor is a receptor for a cytokine, growth factor or other hormone.

11. **(Currently amended)** The method of claim 10 wherein the cell surface receptor is a receptor for erythropoietin ("EPO"), granulocyte colony stimulating factor ("G-CSF"), thrombopoietin ("TPO"), growth hormone ("GH"), interleukin-2 ("IL-2"), interferon-alpha, interferon-beta, or a ~~neurotropic~~neurotrophic factor.

12. **(Previously presented)** The method of claim 8 wherein the biological event is mediated by the association of molecules of two different cell surface receptors and the first and second moieties are different.

13. **(Previously presented)** The method of claim 8 wherein the first and second non-peptidic moieties bind to cytoplasmic portions of the cell surface receptors.

14. **(Previously presented)** The method of claim 8 wherein the first and second non-peptidic moieties bind to extracellular portions of the cell surface receptors.
15. **(Previously presented)** The method of claim 8 wherein the agent binds to the cell surface receptors with a $K_d \leq 10^{-6}$ M.
16. **(Previously presented)** The method of claim 8 wherein the first and second non-peptidic moieties have a molecular weight less than 5 kD.
17. **(Previously presented)** The method of claim 8 wherein the agent is membrane permeant.
18. **(Previously presented)** The method of claim 8 wherein the cell surface receptors are selected from the group consisting of:
epidermal growth factor-receptor (EGF-R),
ataxia telangiectasia and rad-related 2/neuroblastoma oncogene (ATR2/neu),
hermaphrodite homolog-2/neuroblastoma oncogene (HER2/neu),
hermaphrodite-3/cellular-erythroblastic leukemia oncogene homolog-3 (HER3/c-erbB-3),
Xiphophorus melanoma receptor tyrosine kinase homolog (Xmrk);
insulin-like growth factor-I-receptor (IGF-1-R),
insulin receptor-related receptor (IRR);
platelet-derived growth factor receptor-a (PDGF-R-a),
platelet-derived growth factor receptor- β (PDGF-R- β),
colony stimulating factor-1-receptor (CSF-1-R, macrophage-colony stimulating factor-receptor (M-CSF-R)/cellular-McDonough feline sarcoma homolog (c-Fms)),
c-kit (Steel Factor Receptor, mast/stem cell growth factor receptor, HZ4-feline sarcoma virus viral oncogene homolog),
serine/threonine kinase/fms-like tyrosine kinase 2 (STK-1/Flk-2);
fibroblast growth factor-receptor (FGF-R),
[acidic-] fibroblast growth factor-receptor-1 (flg),
[basic-] fibroblast growth factor-receptor-2 (bek);

neurotrophic tyrosine kinases;
 cell-surface determinant-3-z (CD3-zeta)
 cell surface/class II determinant-3-h (CD3-eta);
 β chain of Fc/IgE receptor-1 (FCERI),
 g chain of Fc/IgE receptor-1 (FCERI);
 g chain of Fc receptor/cell-surface determinant-16 (Fc γ -RIII/CD16);
 cell-surface determinant-3-g (CD3-gamma) subunit,
 cell-surface determinant-3-d (CD3-delta) subunit,
 cell-surface determinant-3-e (CD3-epsilon) subunit;
 Ig-a subunit of B-cell antigen receptor complex/membrane-bound,
 Ig-associated protein-1 (Ig-a/MB-1)
 Ig- β subunit of B-cell antigen receptor complex/c membrane-bound,
 Ig-associated glycoprotein B29 (Ig- β /B29);
 the common β subunit shared by the granulocyte/macrophage-colony stimulating factor (GM-CSF), interleukin-3 (IL-3) and interleukin-5 (IL-5) receptors;
 the β chain of glycoprotein MW 130 KD (gp130) associated with the interleukin-6 (IL-6), leukemia inhibitory factor (LIF), ciliary neurotrophic factor (CNTF), oncostatin M, and interleukin-11 (IL-11) receptors;
 the interleukin-2 (IL-2) receptor gamma subunit associated also with receptors for interleukin-4 (IL-4), interleukin-7 (IL-7) and interleukin-13 (IL-13);
 the β chain of the interleukin-2 (IL-2) receptor;
 interferon (IFN) α receptor,
 interferon (IFN) β receptor,
 interferon (IFN) γ receptor;
 growth hormone (GH) receptor,
 erythropoietin (EPO) receptor,
 prolactin receptor; and
 the Transforming growth factor- β (TGF- β) family of cell surface receptors.

19. **(Previously presented)** A method for preparing an agent that effects a biological event mediated by the association of two or more endogenous protein mediators, the method

comprising preparing an agent which includes a first non-peptidic moiety that binds to one of the protein mediators covalently linked with a second non-peptidic moiety that binds to the other protein mediator, wherein the agent binds to both protein mediators, the biological event is mediated by the association of molecules of two different protein mediators and the first and second moieties are different.

20. **(Previously presented)** The method of claim 19 wherein at least one of the protein mediators is a cell surface receptor.

21. **(Previously presented)** The method of claim 19 wherein the two different protein mediators are cell surface receptors.

22. **(Previously presented)** The method of claim 19 wherein the biological event is transcriptional regulation, the first non-peptidic moiety binds to a protein containing a DNA-binding domain and the second non-peptidic moiety binds to a protein containing a transcriptional regulatory domain.

23. **(Previously presented)** The method of claim 22 wherein the transcriptional regulatory domain is a transcriptional activation domain.

24. **(Previously presented)** The method of claim 22 wherein the transcriptional regulatory domain is a transcriptional repression domain.

25. **(Previously presented)** The method of claim 19 wherein the biological event is translocation of a selected protein to a predetermined cellular component, the first non-peptidic moiety binds to the selected protein and the second non-peptidic moiety binds to a constituent of the predetermined cellular compartment.

26. **(Previously presented)** The method of claim 25 wherein the first non-peptidic moiety binds to a protein that functions only in the cytoplasm and the second non-peptidic moiety binds to a constituent of the nucleus or mitochondrion.

27. **(Previously presented)** The method of claim 19 wherein the biological event is destruction of a selected protein, the first non-peptidic moiety binds to the selected protein and the second non-peptidic moiety binds to a constituent of the proteasome.
28. **(Previously presented)** The method of claim 8 or 19 further comprising mixing the agent with a pharmaceutically acceptable carrier and optionally with one or more pharmaceutically acceptable excipients.
29. **(Previously presented)** A method which comprises providing an agent prepared according to the method of claim 8 or 19 and mixing the agent with a pharmaceutically acceptable carrier and optionally with one or more pharmaceutically acceptable excipients.